Intra-Thoracic Actinomycosis Presenting as Empyema

REPORT OF A CASE

By R. A. PYPER, M.D., M.R.C.P.(LOND.)
Royal Victoria Hospital, Belfast.

THORACIC actinomycosis, a comparatively uncommon condition, may arise by direct inhalation of the infecting organism, by metastatic spread from a focus elsewhere, or by infiltration through the œsophagus. It may present as a broncho-pneumonia or as a lung abscess; it may closely simulate pulmonary tuberculosis or spreading suppurative pneumonitis; new growth or bronchiectasis may be suggested; sometimes, as in the present case, there is an empyema. Diagnosis is not usually established until the organism is found in sputum or in pus from a surgically drained abscess; sometimes not until "sulphur granules" appear in pus from one or many discharging sinuses in the chest-wall. If empyema has occurred diagnosis may be made by thoracentesis.

If the progress of the abscess-forming granulomatous lesion remains unchecked the result is disastrous, and in pre-penicillin days few patients survived more than than a year or two. The outlook is now more hopeful, but a definite line of satisfactory treatment does not as yet appear to have been finally decided, particularly with reference to the dosage of penicillin which should be employed, and the length of time for which it should be continued.

REPORT OF CASE

The patient, a district nurse of 43 years, was admitted to the City and County Hospital, Londonderry, on 10th April, 1947, with a diagnosis of pneumonia in the left lower lobe. Intramuscular penicillin, fifty thousand units three-hourly for six days, produced no immediate response, the temperature remaining between 100 and 102°F., but three days later it dropped to normal and remained so for a further three weeks; during this period dullness at the left base, both clinically and radiologically, remained. On the 10th of May, one month after admission, the temperature rose again to 102°F., and failed to respond to a further course of penicillin (twenty thousand units three-hourly for twenty-three days) supplemented by sulphamerazine (1 gramme six-hourly for six days). The clinical signs and radiograms suggested empyema, but diagnostic needling of the chest on three occasions failed to find pus or fluid. Two examinations of sputum showed pneumococci and streptococci; no tubercle bacilli were found direct or on culture. White cell count was fourteen thousand per c.mm.; Hb. was 75 per cent. and blood film showed microcytic hypochromic anæmia.

She was transferred to the Royal Victoria Hospital, Belfast, on 16th June, with a diagnosis of probable interlobar empyema, having maintained for the previous six weeks a swinging temperature between 101 and 103°F., with a corresponding pulse rate and respirations about twenty to twenty-four per minute.

On admission to the Royal Victoria Hospital she was found to be a well-nourished woman with slight pallor of the conjunctivæ. There was no cyanosis, no palpable enlargement of superficial lymph glands, and no œdema; she showed no respiratory distress; there was slight finger-clubbing. The pulse rate was ninety-two per minute and the temperature was 100°F.

Outside the respiratory system nothing of interest was discovered on routine clinical examination.

Examination of the chest revealed diminished expansion of the left side. The trachea was in the mid-line and there was no deviation of the apex beat from its normal position. There was flat dullness to percussion over the left lower lobe and also anteriorly over a wedge-shaped area, its apex towards the sternum, in the left mid-zone extending laterally to the upper half of the left anterior axillary line. Elsewhere percussion resonance was normal. Over all of the dull areas described there was diminished vocal fremitus, increased vocal resonance, bronchial breathing and whispering pectoriloquy. Air entry was diminished at the left base. No adventitious sounds were heard.

Sputum showed nothing of interest. Blood examination gave a white cell count of fourteen thousand two hundred per c.mm., with 83 per cent. neutrophil polymorphs, and confirmed the presence of a moderate degree of microcytic hypochromic anæmia. The B.S.R. was 85 mm. in one hour (Westergren).

The chest was screened and radiograms were taken. In the postero-anterior view the appearances were consistent with a pleural effusion extending up to the mid-zone, but could have been produced by pleural thickening. The lateral picture showed a rounded pear-shaped opacity with smooth outline in the region of the sixth to eighth left ribs far back in the paravertebral gutter, with a vague, irregular, fainter shadow running upwards and forwards from its anterior end, and a third doubtful shadow, largely obscured by the heart, running downwards and forwards in the region of the interlobar fissure.

These appearances and the clinical signs were interpreted as those of an encysted empyema, and the chest was needled in the seventh left interspace between the scapula and the vertebral column. A little blood and one or two c.cm. of thick, almost solid pus were obtained. The pus was too thick for further aspiration. One quarter of a million units of penicillin in 4 c.cm. of saline was injected through the aspirating needle before withdrawl. This procedure was repeated on the following day, and the next day intramuscular injection of penicillin, two hundred thousand units three-hourly, was commenced. Laboratory examination of the pus showed abundant polymorphs and lymphocytes and a few gram-negative bacilli; no tubercle bacilli were seen; culture was sterile.

It was decided to drain the chest by rib-resection, and this was carried out by Mr. G. R. B. Purce on the following day (23rd June). A small portion of the eighth rib was resected on the left side posteriorly, after aspiration of pus through the eighth interspace, and the pleural cavity was opened. There was a good deal of loculation and it was difficult to say if all the trabeculæ were pleural; some appeared to be pulmonary; there were "tunnels" of pus tracking in several direc-

tions; the appearances were reminiscent of the "lattice lung" pictured in Sauerbruch and O'Shaughnessy's book (1937). Many ounces of pus were aspirated and a large drainage tube was inserted.

Microscopical examination of the pus showed polymorphs and lymphocytes and actinomyces. (This was cultured and shown, some two and a half weeks later, to be penicillin-sensitive.)

After operation intramuscular penicillin was continued as before, and in addition one Mega unit was instilled daily into the pleural cavity through the drainage tube. Three days later two grammes of sulphadiazine were given orally, followed by one gramme four-hourly. The day following operation the temperature fell from a previous level of 103°F. to 98.2°F., and thereafter only rose above normal on five occasions over the next eight weeks, and was never above 99°F. Four days later the white cell count fell to six thousand two hundred per c.mm., with 36 per cent. polymorphs: sulphadiazine was discontinued (total thirty-three grammes in six days) and the intra-pleural penicillin was increased to one Mega unit twice daily.

Three days later pus from the drainage tube showed no organisms and was sterile on ærobic and anærobic culture. The patient was now feeling well for the first time in three months and was allowed up out of bed for short periods (eleven days after operation). Thereafter clinical recovery was uneventful, although there was one bacteriological set-back. The dosage of penicillin was now reduced by fifty per cent. to one hundred thousand units intramuscularly three-hourly, and five hundred thousand units twice daily intra-pleurally.

On 7th July, two weeks after operation, Mr. Purce examined her again: there was now no sign of a broncho-pleural fistula, and on coughing the lung came up almost to the chest wall. The large drainage tube was removed and a smaller one substituted. Three days after this the laboratory reported that actinomyces grown in culture from the pus from the original operation was penicillin-sensitive. On 12th July the dosage of penicillin was again halved and it was discontinued on 19th July. (Total dosage: 28.5 million units intramuscularly and 27 million units intrapleurally in thirty days.)

By this time the wound was clean and the lung was expanding well. Five days later a swab from the wound showed the reappearance of actinomyces and penicillin was recommenced: one hundred thousand units three-hourly intramuscularly and five hundred thousand units intrapleurally twice daily. Two days after this (26th July) the drainage tube slipped out. As there was no visible pus and as the lung was expanding well, it was decided not to re-insert it but to allow the wound to heal under a dry dressing. Intramuscular penicillin was continued in the same dosage and five hundred thousand units were infiltrated through the wound and into its edges twice daily. A wound swab showed no organisms on 4th August, and on 8th August penicillin therapy was finally terminated, the total dosage in the second course of sixteen days being twelve million units systemically and fifteen million units locally. Thereafter repeated swabs were negative.

On 18th August there was still a small sinus in the chest-wall with a little serous

discharge. There was dullness and impaired air entry over the left lower lobe; there were no adventitious sounds. The patient looked and felt well and had no cough or other symptoms. She was discharged on this date, eight weeks after operation, having been in hospital for just over four months, and was advised to take a holiday. She had been having iron and ammonium citrate to combat the anæmia and was told to continue this.

She was seen again on 28th August, by which time the sinus had closed; and again on 11th September, 1947, when she looked and felt very fit. The wound was firmly healed. Expansion of the left hemi-thorax was now only very slightly less than the right. There was some impairment of resonance over the left lower lobe, and although air entry was good, it was still a little diminished. There were no adventitiæ. There were no symptoms. The B.S.R. was 4 mm. in one hour. Hb. was 70 per cent; red cells 4,870,000 per c.mm. X-ray of the chest now showed slight dullness only at the left base, with slight elevation of the left diaphragm, and good re-expansion of the left lower lobe. The patient was considered fit to resume work at the end of the month.

Commentary

The dosage of penicillin used in this case was very high: it may have been wastefully so; but a brief glance at the literature on actinomycosis and penicillin reveals potent arguments in favour of intensive and prolonged therapy.

Since Waksman and Woodruff (1942) investigated, *inter alia,* the penicillin-sensitivity of actinomyces, it has been shown (Ministry of Supply, 1945) that most pathogenic strains are penicillin-sensitive, but that sensitivity is variable and some strains are apparently resistant. McGregor (1944) stated that the majority of organisms from human cases of actinomycosis had proved very insensitive to penicillin. Hudson (1946) quotes six cases of actinomycosis treated with sixty thousand units of penicillin intramuscularly three-hourly, of which only one—and this an early case of the cervical type—in which this therapy was continued for twenty-one days, appeared to be cured. The five failures were treated with similar dosage, some for the same, and some for a shorter period. Kolmer (1945), advocating the administration of twenty thousand units of penicillin every four hours, to a total of four million to eight million units, together with sulphonamide therapy, quotes twenty cases of actinomycosis in which there was improvement or recovery in six, and in the remaining fourteen treatment was ineffective. He concludes that "it is highly probable that most cases will require repeated courses of treatment with penicillin, a sulfonamide compound, and iodide over three to five months or longer periods of time."

Fleming (1946) lays down the following four general rules for penicillin treatment:—

"1. It should be used only when there is infection by a penicillin-sensitive microbe." Elaborating this, he points out that sensitivity varies; that certain organisms that are insensitive to concentrations which can be reached in the blood,

are sensitive to the higher concentrations which may be reached by local application; and that in some cases it is permissible to institute therapy before sensitivity tests can be carried out.

"2. Penicillin must be administered in such a way that it comes in contact with the infecting microbe." Under this heading he reminds us that it is easy to introduce penicillin directly into an empyema or other infected cavity in far greater concentration than can possibly diffuse from the blood.

"3. The dose should be such that in the infected area the concentration of penicillin is sufficient to destroy the bacteria." In his discussion on this he mentions that penicillin is the only chemotherapeutic substance which is almost completely non-toxic; that the only reason for limiting the dose is an economic one; and that when there is any doubt it is wise to overdose rather than underdose.

"4. The treatment should be persisted in until the infection is defeated."

In view of the foregoing; the lack of a final decision on the optimum dosage of penicillin in actinomycosis; the impossibility of knowing the degree of sensitivity of the infecting organism until cultures have been made; the very serious and unpleasant results of the unchecked spread of an actinomycotic lesion in the thorax (or elsewhere); and, in this particular case the previous failure of response to sulphamerazine and smaller doses of penicillin, it is felt that Fleming's four rules were best complied with by the method employed, which aimed at getting as high a concentration of penicillin as possible carried by the blood stream to the growing intra-pulmonary granuloma and also a continuous high concentration in the actinomyces-infected pus flooding the pleural cavity, with sulphadiazine in the early stages as an additional weapon of attack. Even with the heavy dosage employed the condition temporarily relapsed on discontinuing penicillin-therapy after thirty days, and only finally cleared after a second shorter and somewhat less intensive course.

A few further points remain to be mentioned:—

The surgical drainage of the pus-filled pleural cavity follows soundly established and generally accepted principles.

Sulphonamides have in the past been found helpful in the treatment of some cases of actinomycosis, and one of this group of drugs was used in this case in addition to penicillin.

McGregor and others (1944) consider that radiotherapy is a useful method of treatment in actinomycosis. Iodides have for years been recommended. Neither of these forms of therapy was used in this case.

I am now of the opinion that the rounded opacity described in the lateral radiogram, which was originally interpreted as being an encysted empyema, was possibly the shadow of an intrapulmonary actinomycotic granuloma—the primary cause of the trabeculated empyema. (This shadow had disappeared when the patient was X-rayed again after treatment.)

Finally, the treatment adopted appears to have resulted in cure.

Summary and Conclusion

A case of intra-thoracic actinomycosis presenting as empyema, and treated by rib-resection with drainage, penicillin, and sulphadiazine, is described.

Penicillin therapy in actinomycosis is discussed: arguments in favour of heavy and prolonged dosage are advanced. In this case a total of eighty-two and a half million units of penicillin was given by systemic and local administration in two courses of thirty days and sixteen days.

Other methods of treatment are briefly mentioned.

A satisfactory result appears to have been obtained.

Most pathogenic strains of actinomyces are penicillin-sensitive, though in varying degree. Actinomycosis would thus seem to be an example of a disease whose prognosis has been markedly altered for the better by the advent of penicillin therapy, provided that adequate dosage is maintained for a sufficient time.

I wish to thank Dr. S. I. Turkington for permission to report this case. Thanks are also due to Mr. G. R. B. Purce, who performed the rib-resection and supervised the subsequent drainage; to Dr. A. L. Wells, who cultured the actinomyces and demonstrated its penicillin-sensitivity; and to Dr. J. W. Dundee, House Surgeon in the City and County Hospital, Londonderry, for the full clinical notes which accompanied the patient from that hospital.

References

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REVIEW

DYING, APPARENT DEATH, AND RESUSCITATION. By S. Jellinek, M.D. Baillière, Tindall & Cox. Pp. 263. 10s. 6d.

This is a textbook of thanatology. It includes chapters on clinical thanatology with reference to remissions and intermissions in the psycho-somatic state, thanatogenesis, scope, and potentialities of the psychium in the dying process, the swallowing phenomenon and its dual thanatological significance and other matters.

Those who are interested in these subjects will no doubt find they are getting full value for their half-guinea. R. W. M. S.